

REMARKS

The undersigned, on behalf of the Applicants, expresses appreciation to Examiner Spivak for the telephonic interviews granted on May 13, 2004 and May 17, 2004. These interviews were helpful in resolving some of the issues in the case and the undersigned believes that they will expedite the prosecution of this case

Applicants and the undersigned are in agreement with the Examiner's comments concerning the timely submission of pertinent references. In this regard, the fact that the Examiner did not have the benefit of reviewing the references cited in the Information Disclosure Statement (IDS) was discussed. While the IDS was mailed on February 18, 2004, prior to the time the first office action was mailed (February 26, 2004), the Examiner was unable to review it prior to that time. Examiner Spivak indicated that the references cited in the IDS will be considered by her before issuing the next office action. In this regard, a supplemental Information Disclosure Statement is enclosed.

The Examiner was also advised that related cases U.S. Applications Serial Nos. 10/651 216, filed August 28, 2003, 10/651 221, filed August 28, 2003, 10/651, filed August 28, 2003 and 10/651 290, filed August 28, 2003 are on file in the Office.

Claims 1 to 21 are in the application.

Claims 5-18 stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1-21 stand rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-21 stand rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

THE REJECTION OF CLAIMS 5-16 UNDER 35 USC 112,
SECOND PARAGRAPH, AS BEING INDEFINITE

The Examiner states that "the formulas designated as VII, VII and IX respectively in claims 5, 9, and 14 lack clear antecedent basis in Claim 1." However, as was pointed out during the interview, Formula VI and its substituent definitions in dependent Claim 2, Formula VII and its substituent definitions in dependent Claim 5, Formula VII and its substituent definitions in dependent Claim 9 and Formula IX and its substituent definitions in dependent Claim 14 are the same as the corresponding formulas and substituent definitions in independent claim 1. The Examiner indicated that this rejection would be withdrawn.

THE REJECTION OF CLAIMS 1-21 UNDER 35 USC 112,
FIRST PARAGRAPH, AS NOT BEING ENABLED BY THE DISCLOSURE

Claim 1, as amended, defines a method for treating inflammatory response associated with atherosclerosis or restenosis in mammals by administering to said mammal an effective amount of a compound selected from the group consisting of structures of Formula VI, Formula VII, Formula VIII and Formula IX. As known by those skilled in the art, inflammatory response precedes atherosclerotic lesions. Support for the language "inflammatory response" can be found on page 23, first full paragraph, of the specification, and hence it does not constitute new matter. Contrary to the Examiner's rejection, these claims are deemed to be enabled by the disclosure.

It is appreciated that the Examiner's first examination of the application was made without benefit of the information contained in the Background of The Invention and the Information Disclosure of the specification. It is hoped that

this information will provided a basis for the Examiner's reconsideration of the 112 first paragraph rejection.

In the first instance "the PTO is required to assume that the specification complies with the enablement provisions of 112 unless it has acceptable evidence or reasoning" to suggest otherwise. *Gould v Mossinghoff*, 229 U.S.P.Q. 1 (D.C. 1985). The Examiner has not set forth reasons as to why the accuracy of applicants statements should be doubted. *In re Marzocchi and Horton*, 169 U.S.P.Q. 367 (C.C.P.A 1971).

The use recited in claims 1-21 is not incredible as is shown by the references cited in the information disclosure statement. In particular, note US Patent No 6 291 437 (the '437 patent) which discloses the use of pharmaceutical compositions for preventing and retarding atherosclerotic lesions or restenosis in mammals.

With respect to the articles regarding animal models referred to in the paragraph bridging pages 55 and 56 of the specification, (Lemstrom et al and Burnell et al), copies of them are included with the supplemental Information Disclosure Statement enclosed.

The compounds used in the claimed methods are clearly defined. Methods for preparing them and pharmaceutical compositions incorporating them are disclosed. Also, dosage forms and modes of administering them are set forth in the specification beginning on page 44, line 5 through page 55, first full paragraph. With respect to the dosage range, it is stated on page 44 of the specification,

"Pharmaceutical compositions, including one or more anti-atherosclerosis or anti-restenosis agents can be administered orally or parenternally at dose levels, calculated as the free base, of each of the anti-atherosclerosis or anti-restenosis agent at 0.1 to 300 mg/kg, preferably 1 to 30 mg/kg of mammal body weight and can be used in a human in a unit dosage form, administered one to four times daily in the amount of 1 to 1,000 mg per unit dose."

Further disclosure of how to use the compounds of Formulae VI, VII, VIII and IX in the claimed method is in the paragraph bridging pages 44 and 45 of the specification.

THE NATURE OF THE INVENTION, STATE OF THE PRIOR ART

The examiner has not explained why the state of the prior art renders the claims non-enabled. As a matter of fact, the cited prior art is replete with discussions about the possible relationship between viral infections and atherosclerosis and restenosis.

RELATIVE SKILL OF THOSE IN THE ART

The undersigned agrees with the Examiner's statement regarding the relative level of skill in the art. However, the Examiner has not stated why this factor renders Claims 1-21 non-enabled.

THE PREDICTABILITY OF THE ART

In making this point, the Examiner states "It is clear in the art to which the the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical activity. However, this statement is not supported by any evidence or reasons of record. Furthermore, the inventors in the '437 patent disclose that laboratory animals, such as rabbits, are well established models for experimental atherosclerosis. (See Example 5, column 13, lines 33-43).

BREADTH OF THE CLAIMS

The Examiner has not specified why the complete breadth of the claims is not supported by the specification. Each limitation recited in the claims is supported by the specification. While it is true that the claims encompass a large number of compounds for use in the claimed methods, the specification teaches modes of administration, dosage forms and doses that are applicable to the compounds.

THE AMOUNT OF DIRECTION OR GUIDANCE PROVIDED
AND THE PRESENCE OR ABSENCE OF WORKING EXAMPLES

Applicant provides guidance by teaching the modes of administration, dosage forms and doses. There is no requirement that a specific example be disclosed. There is also no requirement that guidance be provided as to which compounds are preferred if there is no such preference.

THE QUANTITY OF EXPERIMENTATION NECESSARY

It is assumed that the Examiner cites this factor to suggest that undue experimentation would be involved in practicing the claimed invention. However, she has not explained why such undue experimentation would be required.

The Examiner further states that

"Each particular atherosclerosis or restensis event has its own specific characteristics and etiology. The broad recitation 'treatment or prevention of atherosclerosis or restenosis' is inclusive of many conditions that presently have no established successful therapies."

However, the Examiner has not supported this assertion with any evidence or reason of record. Furthermore, as disclosed on page 23, lines 7-9 of the specification, the condition prevented or treated by the claimed method is the "inflammatory response associated with atherosclerosis or restenosis. Support for this language can be found in the specification, page 2, second full paragraph and page 23, first full paragraph. It is known in the art that arterial lesions result from excessive inflammatory responses. Lamb et al, Infection, immunisation and atherosclerosis: Is there a Link? Vaccine, Volume 17 (1999), pp. 559-564 (copy enclosed).

THE REJECTION OF CLAIMS 1-21 AS FAILING TO COMPLY
WITH THE WRITTEN DESCRIPTION REQUIREMENT

In making this rejection, the Examiner asserts,

"The claim contains subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the applicant, at the time the application was filed, had possession of the claimed invention. ... The specification fails to describe or define the plethora of heterocyclic compounds with the definition of the terms."

This assertion is not supported by the record. In both the Summary of The Invention in the specification and the claims, the term "het" is defined. For example, with respect to Formula IX, the definition of "het" is set forth on page 22, line 22, of the specification and in Claim 1 as follows:

"het is a four-(4), five-(5), six(6) or seven(7) membered saturated or unsaturated heterocyclic ring having 1,2, or 3 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen, which is optionally fused to a benzene ring, or any bicyclic heterocyclic group."

Also, examples of "het" are set forth in Examples 2-5 of US Patent 6 413 958 (The patent in which the compounds of Formula IX are claimed) which is incorporated by reference on page 23, last paragraph of the instant specification. Further, this rejection is not applicable to Claims 4, 7, 8, 12, 13 and 16. These six claims recite specific compounds and are supported by the disclosure. In addition, use of compounds containing heterocyclic groups are enabled just as compounds containing other groups are enabled by the disclosure.

The application discloses specific compounds, modes of administration, dosage forms and doses. Therefore, it meets both the enablement and written description requirement of 35 USC 112, first paragraph. It also complies with the definitions requirement of 35 USC 112, second paragraph.

For the above reasons, withdrawal of the rejections and expeditious passage of the application are respectfully solicited.

Respectfully submitted,



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Encl: Information Disclosure Statement and
Petition for Consideration
Postal Card

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